

Supplementary Table 1. Summary of regional PET retention data at baseline.

¹¹C-PiB and ¹⁸F-FDG PET data are expressed in SUVR with the pons as reference (mean \pm SD for each group). ¹¹C-DED binding is expressed as the ratio of the modified reference Patlak model slope in a ROI (min^{-1}) to that in the cerebellar grey matter ($= 0.01 \text{ min}^{-1}$), expressed as the mean \pm SD for each group. The pMC group comprised subjects who were younger than the AAO ($n = 5$). The sMC group for ¹¹C-PiB retention ($n = 2$) excludes Arctic carriers because of the low ¹¹C-PiB retention in this mutation type. The CTR groups were composed of non-carrier members of ADAD families ($n = 16$) for ¹¹C-PiB and ¹⁸F-FDG PET, and healthy subjects ($n = 14$) for ¹¹C-DED PET.

AAO = average age at onset of symptoms; CTR = control; ¹¹C-DED = deuterium-L-deprenyl; ¹⁸F-FDG = fluorodeoxyglucose; MCI = mild cognitive impairment; ¹¹C-PiB = Pittsburgh Compound-B; pMC = presymptomatic mutation carrier; ROI = region of interest; SD = standard deviation; sMC = symptomatic mutation carrier; SUVR = standardized uptake value ratio.

¹¹ C-PiB retention in ROIs (SUVR to pons)	CTR (n = 15)	pMC (n = 5)	sMC (n = 2)	PiB- MCI (n = 4)	PiB+ MCI (n = 13)	Alzheimer's disease (n = 8)
<u>Cortical regions</u>						
Frontal cortex	0.63 \pm 0.04	0.87 \pm 0.18	1.46; 1.31	0.58 \pm 0.03	1.11 \pm 0.13	1.28 \pm 0.13
Parietal cortex	0.63 \pm 0.05	0.82 \pm 0.14	1.40; 1.32	0.59 \pm 0.02	1.13 \pm 0.15	1.27 \pm 0.18
Temporal cortex	0.65 \pm 0.05	0.77 \pm 0.09	1.47; 1.22	0.60 \pm 0.04	1.06 \pm 0.15	1.16 \pm 0.15
Occipital cortex	0.66 \pm 0.05	0.76 \pm 0.08	1.40; 1.07	0.63 \pm 0.05	0.96 \pm 0.16	1.05 \pm 0.23
Anterior cingulate cortex	0.66 \pm 0.05	0.97 \pm 0.26	1.65; 1.38	0.62 \pm 0.02	1.26 \pm 0.12	1.35 \pm 0.12
Posterior cingulate cortex	0.65 \pm 0.06	0.97 \pm 0.23	1.55; 1.52	0.63 \pm 0.01	1.29 \pm 0.14	1.41 \pm 0.18
Insular cortex	0.68 \pm 0.04	0.87 \pm 0.14	1.53; 1.31	0.65 \pm 0.04	1.12 \pm 0.11	1.19 \pm 0.11
Parahippocampus	0.65 \pm 0.06	0.73 \pm 0.09	1.30; 0.93	0.61 \pm 0.03	0.85 \pm 0.10	0.86 \pm 0.09
<u>Subcortical regions</u>						
Caudate nucleus	0.60 \pm 0.07	1.04 \pm 0.33	1.21; 1.17	0.56 \pm 0.02	1.00 \pm 0.14	1.06 \pm 0.14
Putamen	0.74 \pm 0.05	1.17 \pm 0.36	1.66; 1.73	0.72 \pm 0.03	1.24 \pm 0.15	1.38 \pm 0.11
Thalamus	0.69 \pm 0.07	0.95 \pm 0.28	1.04; 0.98	0.62 \pm 0.02	0.92 \pm 0.09	0.92 \pm 0.09
Hippocampus	0.71 \pm 0.06	0.76 \pm 0.08	1.28; 0.84	0.62 \pm 0.05	0.80 \pm 0.11	0.77 \pm 0.07

¹¹ C-DED binding in ROIs (ratios to cerebellum)	CTR (n = 14)	pMC (n = 5)	sMC (n = 4)	PiB- MCI (n = 4)	PiB+ MCI (n = 13)	Alzheimer's disease (n = 8)
<u>Cortical regions</u>						
Frontal cortex	1.21 ± 0.08	1.40 ± 0.09	1.26 ± 0.04	1.23 ± 0.11	1.33 ± 0.18	1.30 ± 0.14
Parietal cortex	1.15 ± 0.09	1.34 ± 0.10	1.15 ± 0.07	1.18 ± 0.13	1.28 ± 0.15	1.23 ± 0.13
Temporal cortex	1.32 ± 0.11	1.41 ± 0.09	1.28 ± 0.05	1.28 ± 0.11	1.36 ± 0.16	1.29 ± 0.10
Occipital cortex	1.13 ± 0.11	1.26 ± 0.05	1.19 ± 0.07	1.11 ± 0.07	1.24 ± 0.10	1.21 ± 0.14
Anterior cingulate cortex	1.59 ± 0.13	1.76 ± 0.10	1.50 ± 0.08	1.54 ± 0.28	1.58 ± 0.21	1.49 ± 0.13
Posterior cingulate cortex	1.48 ± 0.14	1.73 ± 0.19	1.38 ± 0.18	1.38 ± 0.23	1.56 ± 0.25	1.48 ± 0.15
Insular cortex	1.55 ± 0.13	1.69 ± 0.15	1.46 ± 0.10	1.48 ± 0.12	1.54 ± 0.20	1.46 ± 0.11
Parahippocampus	1.42 ± 0.19	1.48 ± 0.10	1.25 ± 0.80	1.33 ± 0.09	1.47 ± 0.19	1.38 ± 0.07
<u>Subcortical regions</u>						
Caudate nucleus	1.77 ± 0.27	2.11 ± 0.42	1.65 ± 0.16	1.72 ± 0.23	1.84 ± 0.33	1.65 ± 0.29
Putamen	2.28 ± 0.28	2.37 ± 0.13	2.08 ± 0.13	2.14 ± 0.20	2.24 ± 0.29	2.19 ± 0.18
Thalamus	1.98 ± 0.26	2.40 ± 0.02	1.96 ± 0.11	2.04 ± 0.20	2.09 ± 0.27	1.87 ± 0.29
Hippocampus	1.63 ± 0.20	1.70 ± 0.16	1.50 ± 0.90	1.67 ± 0.16	1.67 ± 0.26	1.52 ± 0.90

¹⁸ F-FDG uptake in ROIs (SUVR to pons)	CTR (n = 16)	pMC (n = 5)	sMC (n = 4)	PiB- MCI (n = 4)	PiB+ MCI (n = 13)	Alzheimer's disease (n = 8)
<u>Cortical regions</u>						
Frontal cortex	1.57 ± 0.11	1.57 ± 0.11	1.31 ± 0.15	1.41 ± 0.10	1.41 ± 0.09	1.36 ± 0.12
Parietal cortex	1.56 ± 0.10	1.54 ± 0.11	1.23 ± 0.17	1.42 ± 0.10	1.40 ± 0.10	1.31 ± 0.08
Temporal cortex	1.44 ± 0.08	1.43 ± 0.09	1.20 ± 0.11	1.31 ± 0.05	1.27 ± 0.08	1.22 ± 0.06
Occipital cortex	1.62 ± 0.10	1.61 ± 0.12	1.40 ± 0.10	1.52 ± 0.11	1.49 ± 0.13	1.50 ± 0.10
Anterior cingulate cortex	1.49 ± 0.11	1.46 ± 0.10	1.31 ± 0.16	1.36 ± 0.13	1.37 ± 0.12	1.33 ± 0.08
Posterior cingulate cortex	1.73 ± 0.10	1.66 ± 0.10	1.32 ± 0.20	1.49 ± 0.21	1.53 ± 0.11	1.44 ± 0.14
Insular cortex	1.48 ± 0.09	1.46 ± 0.09	1.29 ± 0.10	1.32 ± 0.08	1.33 ± 0.09	1.32 ± 0.08
Parahippocampus	1.18 ± 0.07	1.18 ± 0.05	1.03 ± 0.10	1.06 ± 0.09	1.09 ± 0.07	1.08 ± 0.08
<u>Subcortical regions</u>						
Caudate nucleus	1.43 ± 0.16	1.49 ± 0.21	1.13 ± 0.15	1.27 ± 0.07	1.22 ± 0.11	1.19 ± 0.16
Putamen	1.78 ± 0.16	1.76 ± 0.12	1.62 ± 0.18	1.67 ± 0.12	1.65 ± 0.10	1.69 ± 0.09
Thalamus	1.46 ± 0.12	1.52 ± 0.13	1.26 ± 0.06	1.25 ± 0.18	1.32 ± 0.09	1.24 ± 0.09
Hippocampus	1.19 ± 0.07	1.20 ± 0.05	1.04 ± 0.14	1.08 ± 0.14	1.07 ± 0.07	1.04 ± 0.10